PROCESS FOR THE DEHYDROFLUORINATION OF AN AROMATIC

CARBAMOYL FLUORIDE

A subject matter of the present invention is a process

5   which makes possible the treatment of an aromatic

carbamoyl fluoride to result in the corresponding

isocyanate.

A more particular subject matter of the

present invention is a process of the preceding type

10 which makes it possible to obtain a good degree of

conversion, a good conversion yield, that is to say a

good selectivity, and a good reaction yield.

Carbamoyl fluorides are rather uncommon

compounds which have, however, experienced renewed

15 interest because of the growing role of fluorinated

derivatives in pharmacology and agrochemistry. This is

because one of the most conventional techniques for

synthesizing derivatives exhibiting a perfluorinated

aliphatic carbon consists in blocking possible anilines

20 in the form of an isocyanate, in chlorinating

(generally the alkyl derivative position by means of

radical chlorine, and then treating the chlorinated

derivative obtained with a fluorinated medium,

generally a medium comprising hydrofluoric acid in the

25 liquid phase. During this type of process, the first

reaction which takes place is the addition of hydro-

fluoric acid to the isocyanate functional group to give

a carbamoyl fluoride.

This carbamoyl fluoride is very difficult to convert into isocyanate. This is a great pity as the isocyanate is a very reactive intermediate which makes possible numerous syntheses and which in particular makes possible ready release of the corresponding aniline.

The first part of the reactions is disclosed in various documents and in particular in the document EP-A 152 310 and the document EP-A 129 214. As regards the conversion of the carbamoyl fluoride to the isocyanate, British patent No. 955 898, published on April 22, 1964, on behalf of Bayer, indicates the possibility of carrying out this reaction, in particular in example 1. However, the technique used results in a low yield (35%), the reaction apparently being very difficult and resulting in particular in heavy products described as resins.

This is why one of the aims of the present invention is to provide a process which makes possible the conversion of carbamoyl fluoride to an isocyanate functional group under operating conditions which are easy to employ and which makes possible good reaction yields and good selectivity.

One of the main difficulties encountered during the study which led to the present invention is the very high reactivity of carbamoyl fluoride with

respect to itself or with respect to rich aromatic rings.

These aims and others which will become apparent subsequently are achieved by means of a

5 dehydrofluorination process which makes it possible to convert an aromatic carbamoyl fluoride to an isocyanate, in which process said carbamoyl fluoride is subjected to a temperature at least equal to 80°C, advantageously at least equal to 90°C, in a solvent and

10 that, at said temperature of at least 80°C, said carbamoyl fluoride is in the dissolved or finely dispersed state in said solvent.

According to the present invention, it has thus been possible to demonstrate that the finely

15 dispersed nature or the dissolved nature of the carbamoyl fluoride at a temperature where it is reactive plays a key role in the production of the isocyanate with a good yield.

The reaction will preferably be carried out

20 at a temperature at most equal to 150°C.

Said solvent exhibits a boiling point (starting boiling point in the case of a mixture) advantageously of at least 100°C, more preferably of at least 120°C.

25 It is preferable to arrange for the pressure in the reactor to be such that the solvent is boiling (that is to say, in the great majority of cases, at

reflux). A pressure greater than atmospheric pressure will thus be chosen if the solvent exhibits a boiling point lower than the temperature at which it is desired to operate and a pressure lower than atmospheric

5 pressure will thus be chosen when the solvent has a boiling point higher than the temperature at which it is desired to operate.

According to one of the preferred implementations of the present invention, the solvent,

10 which can moreover be a mixture of solvents, is chosen from those which are miscible with hydrofluoric acid.

This miscibility can be partial or complete but it is preferable for the miscibility to be such that the solvent, or the mixture of solvents, chosen

15 exhibits an ability to dissolve the hydrofluoric acid which is at least equal to 5% by volume, preferably at least equal to 10% by volume. This solubility is of considerable advantage as this miscibility of the solvent with hydrofluoric acid makes it possible to use

20 the latter as third solvent, facilitating the dissolution of the carbamoyl fluoride in the reaction mixture.

Consequently, according to a preferred form of the present invention, hydrofluoric acid is used to

25 facilitate the introduction of the carbamoyl fluoride into the reaction mixture. This introduction can be carried out at low temperature or can be introduced at

high temperature. During the heating or during the

introduction, when the carbamoyl fluoride is introduced

into a solvent heel, the hydrofluoric acid which helps

in the dissolution is removed but, on being removed, it

5 leaves the carbamoyl fluoride in a form which is either

highly divided or even dissolved in the solvent used.

According to a preferred embodiment, during

the introduction of the carbamoyl fluoride, the ratio

of the hydrofluoric acid to the carbamoyl fluoride (HF

10 to carbamoyl fluoride ratio) is at least equal to 2,

advantageously to 3, preferably to 4.

According to one of the preferred

implementations of the present invention, the addition

of carbamoyl fluoride is carried out in the form of a

15 solution of the latter in hydrofluoric acid, the ratios

indicated above being observed.

The best results obtained correspond to the

addition of a solution of carbamoyl fluoride to a

solvent heel which is at the reaction temperature.

20 This solution is advantageously a solution in

hydrofluoric acid, as indicated above.

In the case of an addition to a solvent heel,

the addition must be carried out so as to control the

ratio of the hydrofluoric acid present in the reaction

25 medium, in this specific case including that added,

more exactly in equilibrium with the carbamoyl

fluoride, to the substrate.

In other words, the ratio of the hydrofluoric
acid [the free hydrofluoric acid and that added to an
isocyanate functional group (that is to say, in the
form of carbamoyl fluoride)] and the isocyanate

5 functional groups, real or masked in the carbamoyl
fluoride form, is advantageously at most equal to 5,
preferably at most equal to 0.3, more preferably at
most equal to 0.1. This condition implies a relatively
slow addition of the carbamoyl fluoride.

10 According to the present invention, it is
particularly advantageous to avoid the presence of
impurities having a chlorine in the benzyl position as,
in the context of this reaction, these impurities
appear to be highly reactive and would destroy a number

15 of substrates or compounds deriving therefrom.

By way of indication, it is preferable for
the number of molecules carrying chlorine in the benzyl
functional group to be at most equal to 0.5 to 5%,
advantageously to 2%, preferably to 1%, of the

20 carbamoyl fluorides to be treated.

The substrates which are most suitable for
the present invention are carbamoyl fluorides which
comprise an aliphatic carbon with sp^3 hybridization
carrying at least two fluorines. This aliphatic carbon

25 is generally a benzyl carbon, that is to say that it is
attached directly to an aromatic ring. However, it can
be attached to the aromatic ring via a chalcogen (in

particular oxygen).

The present invention is particularly suited to the case where said aromatic ring is that carrying the nitrogen of the carbamoyl functional group.

5   Such a substrate can comprise several of these aliphatic carbons carrying at least two fluorines.

Thus, the substrate advantageously corresponds to the formula:

10     $$(R)_m-Ar(-(CX_2)_p-EWG)-NH-CO-F$$
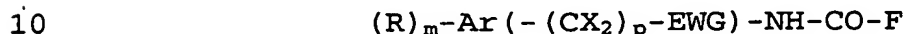
where:

□ Ar means an aromatic residue advantageously exhibiting at least one, preferably two, more particularly three, of the following characteristics:

15   - the residue is mononuclear, that is to say comprises only one ring;

- the residue is advantageously homocyclic;

- the residue has six ring members;

□ the X units, which are alike or different, represent

20   a fluorine or a radical of formula C_nF_{2n+1} with n an integer at most equal to 5, preferably to 2;

□ p represents an integer at most equal to 2;

□ EWG represents a hydrocarbonaceous group or an electron-withdrawing group, the optional functional

25.   groups of which are inert under the reaction conditions, advantageously fluorine or a perfluorinated residue of formula C_nF_{2n+1} with an

integer at most equal to 8, advantageously to 5.
The total carbon number of $-(CX_2)_p-EWG$ is
advantageously between 1 and 15, preferably between 1
and 10.

5 □ m is 0 or an integer chosen within the closed range
(that is to say, comprising the limits) 1 to 4;

□ R is a substituent which is inert under the operating
conditions and which is advantageously chosen from
halogens, advantageously light halogens (that is to
10 say, chlorine and fluorine), and hydrocarbonaceous
radicals, preferably alkyl, aryl, alkylchalcogenyl
(such as alkyloxy) or arylchalcogenyl (such as
aryloxy) radicals.

The substrate compound can in particular have
15 the formula (the optional substituents inert under the
reaction conditions are not displayed):
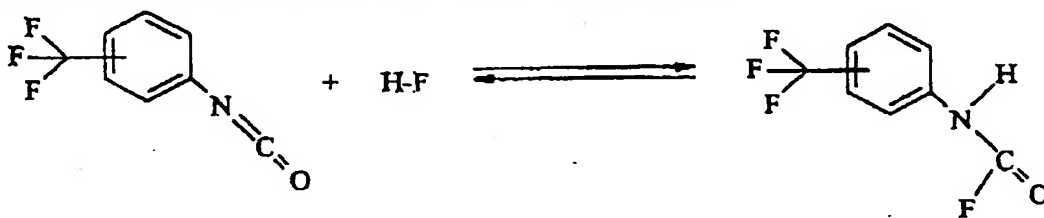
Advantageously, R is an aryl or alkyl
hydrocarbonaceous radical, advantageously with at most
20 10 carbon atoms, preferably with at most 5 carbon
atoms, R can also be carboxyl functional groups,
nitriles, ketones and fluorocarbonyls.

The preferred substituents are either
nothing, that is to say hydrogen, or aryls or alkyls or

alkyloxys.

R or at least one of the R groups can also be a group comprising a carbon carrying at least two fluorines, of formula CX_{2p}-EWG as above.

5   The following examples illustrate the invention.

Example 1

Elimination of hydrofluoric acid in a solvent capable of dissolving the carbamoyl fluoride

10   The solid carbamoyl fluoride (0.1 mol) is charged to a 180 ml Teflon reactor capable of withstanding hydrofluoric acid which is heated by a regulated oil bath and is magnetically stirred. Trichlorobenzene (chlorinated in the 1, 3 and 4 position)

15 is then charged in an amount of 100.4 g.

This results in a suspension easily to be heated. The medium is gradually heated to 80°C and becomes homogeneous, translucent and orange yellow. Evolution of gas begins in the vicinity of 100°C and

20 becomes significant from 105°C. The temperature is raised to 125°C and heated for 7 hours. After cooling, a mass corresponding to an isolated yield of 80% is recovered.

The compound is subsequently subjected to

25 distillation and a yield of 73% in solution in trichlorobenzene is recovered, some resins remaining in the distillation residue.

Example 2

Different tests were carried out using mono-
chlorobenzene as solvent according to various
procedures. The most commonly employed procedure is as
5 follows:

A) Preparation of the carbamoyl fluoride solution

HF is introduced into a reactor at a temperature of
-5°C. The trichloromethylphenyl isocyanate which it
is desired to convert is then introduced at the
10 desired fluorination temperature; the fluorination
lasts 1 h 30, unless indicated otherwise in the
subsequent table, and a finishing operation is
carried out for 4 h at the temperature indicated in
the table. It will be observed that, when everything
15 is otherwise the same apart from the finishing
temperature, the yields are better when the finishing
temperature is brought to a relatively high
temperature, that is to say approximately 20-25°C.
This phenomenon shows the extremely harmful effect of
20 small amounts of derivatives remaining chlorinated
just the once in the benzyl position.

B) Reversion to isocyanate

The carbamoyl fluoride solution, which may or may not
have been subjected to removal of HF beforehand, is
25 introduced into a reactor under the conditions
specified in the table below. The heating, pressure
and temperature conditions are also specified in the

table.

The results are collated in the following table:

No. of the test	HF 07	HF 08	HF 09	HF 10	HF 11	HF 12	HF 13	HF 14	HF 15	HF 16
Fluorination temperature	-5°C	-5°C	-5°C	2°C	2°C	2°C	2°C	-5°C	-5°C	-5°C
Finishing temperature	2°C	2°C	20°C	20°C	20°C	20°C	20°C	20°C	25°C	25°C
HF removal beforehand	No	Yes	No	Yes	No	No	No	No	Yes	Yes
HF released during the distillation-reaction	10	10	10	4.99	4.93	5.72	9.87	8.93	3.72	3.34
Pressure	Atmos-pheric	Atmos-pheric	Atmos-pheric	Vacuum (300 mm)	Vacuum (300 mm)	Atmos-pheric	Atmos-pheric	Atmos-pheric	2 atm	2 atm
Batch or Semi-continuous	Semi-cont.	Batch	Semi-cont.	Batch	Semi-cont.	Semi-cont.	Semi-cont.	Semi-cont.	Semi-cont.	Semi-cont.
Running onto MCB (duration)	1h 45		0 4h		0 2h	4h	4h	4h	4h	4h
Temp, starting-final	130-130°C (reflux)	20-130°C (reflux)	130-130°C (reflux)	48-100°C (reflux)	100-100°C (reflux)	130-130°C (reflux)	130-130°C (reflux)	130-130°C (reflux)	140-150°C (reflux)	130-130°C (reflux)
Duration of the rise	None	3h	None	1h	None	None	None	None	None	None
Duration of the maintenance	2h 30	3h	2h		0	0 2h	2h	2h	2h	2h
Mole, starting	1.67	1.67	1.67	1.66	1.66	1.63	1.67	1.86	1.86	1.67
Mole before distillation	1.18	1.35	1.51	1.42	1.35	1.35	1.55	1.46	1.43	1.36
COF$_2$ evolution	0.05	0.05	0.05	0.09	0.09	0.08	0.06	0.7	0.11	0.1

Yd	70.66%	80.84%	90.42%	85.54%	81.33%	82.82%	92.81%	78.49%	76.88%	81.44%
Distillation Yd	99.00%	84.00%	93.00%	100.00%	85.00%	97.00%	90.00%	100.00%	104.00%	95.00%
Total Yd after distillation	70.00%	68.00%	84.00%	85.00%	76.00%	80.00%	83.00%	79.00%	80.00%	78.00%
Distribution of the light compounds in the final reaction mixture before distillation										
Carbamoyl fluoride			0.70%	3.00%	1.43%	0.47%	0.34%	2.30%	1%	4.50%
Dimer			0.90%	2.50%	1.60%	1.10%	0.98%	0.80%	1%	0.90%
Urea			1.10%	2.00%	1.00%	2.50%	1.60%	1.00%	1%	1.30%
Biuret			6.60%	12%	12.40%	10.00%	7.10%	10.50%	16%	15.10%
Isocyanate	82.93%	77.59%	90.70%	80.50%	83.57%	85.93%	89.98%	85.40%	81%	78.20%
Isocyanate/biuret ratio			13.74242424	6.708333333	6.739516129	8.593	12.67323944	8.133333333	5.0625	5.178807947

Comment on the above results

Tests HF 07 and HF 08, although not really bad, give a relatively mediocre yield of final isocyanate. The explanation of this phenomenon is related to the low finishing temperature, which leaves a not insignificant proportion of greater than 2 or 3% of monochlorodifluoromethylphenyl.

Another reason why test HF 07 is mediocre is the speed with which the carbamoyl fluoride solution is run in, which operation lasts only 1h 45, whereas, in the other cases, it lasts significantly longer.

For tests HF 07 and HF 08, data on the impurities are lacking and consequently not very much can be concluded therefrom. For the tests for which this data is present, the isocyanate/biuret ratio can be used as an index of the selectivity of the reaction.

The reaction HF 09 gives very good results, both with regard to the overall yield and with regard to the purity of the product obtained. This demonstrates the advantage, first, of adding the carbamoyl fluoride in a form dissolved in hydrofluoric acid and, secondly, of operating with a high HF/ carbamoyl fluoride ratio. In that case, the HF/ isocyanate ratio is 10, which corresponds to the hydrofluoric acid/carbamoyl fluoride ratio of 9. The results of tests HF 10 and HF 11 under vacuum are certainly good but slightly disappointing in view of the fact of

having operated under vacuum. However, the rate of addition or the rate of temperature rise was doubtless a little too high.

Test HF 12 is very similar to test HF 09 but
5   the difference with the latter results from the lower content of hydrofluoric acid in the mixture, more exactly the solution added.

In test HF 13, high levels of hydrofluoric acid are again found and thus a much better selectivity
10 of the reaction.

Tests HF 15 and HF 16 show the effect of the increase in the pressure, which is not very favorable.